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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/447,218	11/23/1999	A.K. GUNNAR ABERG	4821-362	3537

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/447,218	Applicant(s) ABERG ET AL.	
	Examiner L. E. Crane	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/23/01(amdt D)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-40,48 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-40,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and the finality of that action is withdrawn.

No claims have been cancelled, amended forms of claims **35 and 37** have been entered, and new claims **48 and 49** have been added as per the amendment filed April 23, 2001. Under the authority of 37 C.F.R. §1.126 claims 41 and 42 have been renumbered as claims **48 and 49** in view of the previous cancellation of claims originally submitted.

Claims **34-40 and 48-49** remain in the case.

Claims **35, 36, 37, 48 and 49** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims **35, 37 and 48** fail to further limit independent claim **34** because the stated limitations in each claim are not accompanied in either claim by a further procedural step or steps. In particular claim **37** also fails to further limit because it fails to identify the particular drug or drugs for which avoidance of interaction is intended. And additionally claim **36** is indefinite for failure to define which particular "cancer/cancers" is/are to be avoided, an important question in light of the wide variation in the severity and etiology of neoplastic disease conditions. Also claims **36 and 49** are incomplete for failure to specify the step or steps to be taken to determine the particular hosts who should avoid the instant method of treatment.

Applicant's arguments with respect to claims **35, 36, 38, 48 and 49** have been considered but are moot in view of the new grounds of rejection.

Claims **35, 36, 37, 48 and 49** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In re claim **35 and 48** applicant has failed to overcome the description clearly present in the Villani et al. '716 patent that DCL and the fluoro analogue thereof do not generate CNS side effects and are also non-sedating: see Villani at column 10, lines 38-44, Table 2 and

associated text. In addition, example 5 (page 24 et seq.) fails to present convincing evidence that the conclusion stated at page 25, lines 34-36 that " ... DCL is less active than terfenadine in inhibiting the cardiac-delayed rectifier and this has no potential for cardiac side effects." Terfenadine is known to cause cardiac side effects (See **Bocian**, PTO-892 ref. **U**, second full paragraph at third page), but is not closely related structurally to DCL (structures found as entries 4239 and 2939, respectively, in The Merck Index, 13th Edition), leading Examiner to wonder why applicant chose to make this comparison in view of the statement concerning a close structural relative of DCL in the noted portion of Bocian: " ... **loratidine** [has] an excellent safety record" (emphasis in original). Therefore, claims **35 and 48** are deemed to lack adequate support from the instant written description and from within the prior art of record.

In re claims **36 and 49** applicant's Example 4 beginning at page 23 fails to provide a convincing factual basis for applicant's conclusion (p. 24, lines 24-25) that " DCL is 5-7 fold less active than loratidine at promoting tumor growth." There is also no apparent prior art basis (art recognized test protocol, etc.) within the disclosure providing either an explanation or other rationale in support of applicant's conclusion. Therefore, examiner concludes that the written description is inadequate to support the subject matter of the noted claims.

Claim **37** is not adequately supported by the written description, particularly Example 6 beginning at page 26. This example appears to be entirely prospective, thereby rendering the instant claim lacking in any factual support whatsoever.

Applicant's arguments with respect to claims **35, 36, 37, 48 and 49** have been considered but are moot in view of the new grounds of rejection.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **34-40, 48 and 49** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Berkow et al.** (PTO-892 ref. **R**) in view of **Villani et al. '716** (PTO-1449 ref. **AE**).

The instant claims are directed to the treatment of urticaria (aka hives) by the administration of an effective dosage of descarboethoxyloratadine (DCL) to a patient in need thereof. The dosage is further defined as 0.1 mg to less than about 10 mg per day or less than about 5 mg per day.

Berkow et al. discloses at p. 333, beginning in the third line under "**Treatment**," that " [s]ymptoms [of urticaria] usually can be relieved with an oral [dose of an] antihistamine ... ."

Villani et al. '716 discloses at column 1, lines 39-46 that descarboethoxyloratadine (DCL) and closely related compounds are effective antihistamines with the advantage of low CNS-related side effects, i.e. that DCL and relatives are non-sedative. Villani also discloses at column 8, lines 11-46 that the dosage range is about 1 mg to 40 mg for a 24 hour period and preferably from about 5 to about 10 mg over this time period (column 8, line 19) More generally the unit dosage is defined as "from 1 mg to 1000 mg according to the particular application" (column 8, lines 43-44).

The findings that
i) Villani et al.'s teaching that DCL and related compounds are known to be effective antihistamines,
ii) the teaching by applicant that DCL has the expected effect in the treatment of urticaria (hives) as predicted by Berkow et al.,
iii) the teaching of dosages ranges which overlap with the claimed dosage ranges, and
iv) the failure of applicant to establish any unexpected results,
when taken together with the disclosure of Berkow et al. are deemed to establish that combination of the instant combination of references is properly motivated. These particular disclosures are also deemed to render the instant claimed subject matter lacking in any patentable distinction in view of the noted prior art.

Therefore, the instant claims directed to treatment of urticaria by the administration of the antihistamine DCL, including within the dosage ranges of the instant dependent claims, would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Applicant's arguments with respect to claims **34-40 and 48-49** have been considered but are deemed to be moot in view of the new grounds of rejection.

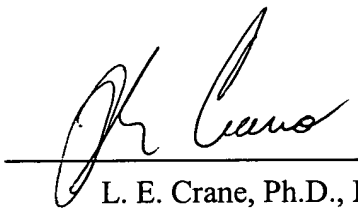
Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX directly to Examiner's computer is 571-273-0651. Telephone numbers for alternative FAX machines operated by Group 1600 are **presently unavailable**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
03/08/2004



L. E. Crane, Ph.D., Esq.
Patent Examiner
Technology Center 1600

Wilson, James

Subject: 103 in Brief 09/447,218

Claim 34 is drawn to treating uticaria with DCL or a pharmaceutically acceptable salt. Claim 35 further limits claim 34 by asserting an additional result of administration of DCL which involves a reduction or avoidance of adverse side effects. Claim 35 attempts to further define the population intended to receive said therapy for uticaria by limiting the human recipient to individuals with a higher propensity or incidence for cancer. Claim 37 introduces an additional limitation to the method of claim 34 which involves the requirement that the active agent avoid interaction with an additional drug, specifically a cytochrome P450 drug. Claims 38-39 delimit the ultimate range of the active agent to be used in the method of claim 34. Claims 48 and 49 further limit claim 35, designating the specific adverse effects intended to be reduced or avoided.

Further limitations your art/rejection should specifically address include:

1. Avoiding side effects;
   Further limitation which is not accompanied by further procedural steps. In the absence of further steps or procedures, the claim is not seen to be sufficiently further limiting of the method of the independent claim.

2. Identity of the recipient of therapy;
   The prior art does not limit the identity of the recipient for therapy and is seen to encompass the population of recipients designated by applicant in the instant claims.

3. Co-administration effects;
   Further limitation which is not accompanied by further procedural steps. In the absence of further steps, procedures or the identity of the drug for which avoidance of interaction is intended, the claim is not seen to be sufficiently further limiting of the method of the independent claim.

4. The range of the DCL to be administered in the prior art;
   Seen in Villani et al column 8, lines 42-46.

5. The adverse effects which will be avoided or reduced.
   Active agent is recognized as non-sedating antihistamine. Sedating antihistamine adverse effects would not be expected.